

In re: Hanley-Bowdoin et al.  
Attorney Docket No. 5051.458  
Application Serial No.: 09/289,346  
Filed: April 9, 1999

Q3  
Cave  
b) regenerating a transgenic plant from said plant cell, wherein expression of said nucleic acid encoding a mutant AL1 protein increases resistance of said plant to infection by at least one geminivirus, compared to a control plant.

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#### REMARKS

Claims 42-48 and 50-54 are pending in this application. Claims 42-48 and 50-54 are canceled herein without prejudice. The specification is amended herein to include Sequence Identifiers for each mutant set forth in Table 3, according to the Sequence Listing as originally filed with this specification. The paragraph on page 39, lines 18-28, is amended herein to correct some obvious inadvertent typographical errors. An Appendix entitled "Marked-up version showing changes made" is attached hereto. New claims 60-77 are added herein to replace claims 42-48 and 50-54, for clarity to more particularly define the invention. New claims 78-86 are added herein to recite methods of using the compositions of claims 60-77, which claims are believed to contain allowable subject matter, and applicants request examination of these method claims in this application as provided according to the rules of rejoinder as set forth in the MPEP in section 821.04. Support for these amendments and new claims is found in the language of the original claims and throughout the specification, as set forth below. It is believed that no new matter is added by these amendments and new claims. Applicants respectfully request entry of these amendments and new claims and reconsideration and allowance of this application in light of these amendments and new claims and the following remarks.

Applicants acknowledge that currently pending claims 42, 47, 48, 50, 51 and 54 are allowed.

In re: Hanley-Bowdoin et al.  
Attorney Docket No. 5051.458  
Application Serial No.: 09/289,346  
Filed: April 9, 1999

## **I. Objection to claims**

The Office Action states that claims 44-46 and 53 are objected to under 37 C.F.R. § 1.75(c) as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. The Office Action goes on to state that the applicants are requested to cancel the claims, amend the claims to place them in proper dependent form or rewrite the claims in independent form. The Office Action further states that it is unclear whether the specific limitation of the claim (such as trans-dominant negative mutant in claim 44) is in addition to the limitations of claim 42, on which it depends and that if it is not subject to the limitations of claim 42, then claim 44 fails to further limit claim 42. The Office Action finally states that these objections would be obviated by amending the claims to recite specific SEQ ID NOs, as appropriate for the claim.

Claims 44-46 and 53 are canceled herein without prejudice, thereby rendering this objection moot and applicants respectfully request its withdrawal.

## **II. Rejection under 35 U.S.C. § 112, second paragraph**

The Office Action states that claim 43-46 and 53 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly needing correction or clarification. Specifically, the Office Action states that in claim 43, the "A" should be removed, in claims 44-46, it is unclear whether all sequences in claim 42 are trans-dominant negative or whether the trans-dominant negative AL1 protein of claim 44 is in addition to the mutation of claim 42, and that claim 53 has a similar problem. Particularly with regard to claim 53, the Examiner asks if the AL1 protein with increased repression of transcription is in addition to the trans-dominant negative mutant AL1 protein of claim 42 or if this is further characterizing of the sequences listed.

In re: Hanley-Bowdoin et al.  
Attorney Docket No. 5051.458  
Application Serial No.: 09/289,346  
Filed: April 9, 1999

Claims 43-46 and 53 are canceled herein without prejudice, thereby rendering this rejection moot and applicants respectfully request its withdrawal.

### **III. Rejection under 35 U.S.C. § 112, first paragraph**

The Office Action states that claims 44-46, 52 and 53 remain rejected under 35 U.S.C. § 112, first paragraph, for reasons of record and that the rejection is maintained since no traversal was presented.

The previous Office Action (dated January 15, 2002) stated that claims 42-47 and 50-54 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement for nucleic acid constructs without the nucleotide sequences encoding the SEQ ID NOs. Specifically, the previous Office Action stated that applicants' invention relates to transgenic plants with increased resistance to geminivirus infection and that the mutants of the AL1/Ca geminivirus protein are useful for producing such plants. The Office Action goes on to state that the invention is to mutants and the nature of the art is such that mutants which result in a predictable desired phenotype are unpredictable. The previous Office Action further stated that it is highly unlikely that any random deletion, substitution, or combination thereof of any number of bases will result in a mutant having reduced binding in the Rb binding region and that it is even more unpredictable to generate trans-dominant mutants since it is known that most mutations in a gene would not result in a mutant which has a trans-dominant negative effect when compared to wild-type. The Office Action continues by stating that it is also highly unpredictable what mutation or combinations of mutations would result in a mutant AL1 protein having increased repression of transcription without further guidance, and that other than the mutants encoded by the sequence identified by the SEQ ID Nos. in the specification, it is unclear how one skilled in the art can predictably generate other mutant AL1 proteins having reduced Rb binding and trans-dominant negative mutants having mutations in the oligomerization domain, the DNA cleavage domain, or the ATPase domain without

In re: Hanley-Bowdoin et al.  
Attorney Docket No. 5051.458  
Application Serial No.: 09/289,346  
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excessive burden and undue experimentation. The Office Action also states that applicants have provided no guidance as to how one skilled in the art can predictably generate trans-dominant mutants in any domain- oligomerization, DNA cleavage, or ATPase- without excessive burden and undue experimentation and that while one of skill in the art can readily make mutations, one needs to know what mutations to make that would have the desired phenotype before the mutations can be made without undue experimentation. The Office Action goes on to state that the applicants have provided no guidance on how to predictably eliminate inoperable embodiments from a virtually ad infinitum of possibilities other than by random trial and error, which is an invitation to experiment and does not fully enable the invention as commensurate in scope with the claims. Finally, the Office Action states that it is suggested that applicants recite the mutants having the specific SEQ ID No. identifiers in these claims.

Claims 44-46, 52 and 53 are canceled herein without prejudice, thereby rendering this rejection moot and applicants respectfully request its withdrawal.

#### **IV. Amendment of Table 3 and page 39 in the specification**

Table 3 on page 23 of the specification is amended herein to complete the list of sequence identification numbers in the column provided therefor. Table 3 as originally filed lists 14 mutants of this invention by name and amino acid substitution and includes a column for the sequence identification number for each mutant. Although a Sequence Listing was filed with this application that provides the amino acid sequence for all 14 mutants listed in Table 3, the SEQ ID NO. column of this table was not filled in when this application was filed. This table is amended herein to complete this column. Support for this amendment is found in the Sequence Listing of the specification, which provides 16 total sequences and identifies them by number, and throughout the specification, wherein the mutants of this invention, as set forth in Table 3, are described.

In re: Hanley-Bowdoin et al.  
Attorney Docket No. 5051.458  
Application Serial No.: 09/289,346  
Filed: April 9, 1999

The paragraph on page 39, lines 18-28 of the specification is amended herein to correct some obvious inadvertent typographical errors and no new matter is believed to be added by these amendments. Applicants respectfully request entry of these amendments into the specification.

#### **V. New claims 60-77**

New claims 60-77 are presented herein to replace previously pending claims 42-48 and 50-54, for clarity in order to more particularly define the claimed invention. In particular, upon review of the claims as previously pending, it appeared that some of the mutants were described incorrectly as having certain phenotypes and the mutants as presented in new claims 60-77 are described correctly for the mutant phenotype recited in the claim. Support for the description of each mutant listed in each claim as having the phenotype recited in that claim is provided at various places in the specification and in particular in the Figures and in the Examples section presented therein. For example, mutants that inhibit binding of AL1 protein to a plant Rb protein, as recited in new claims 60, 67 and 73, are described on page 37, lines 24-31 of the specification, wherein seven mutants (SEQ ID NO:2 (Ala1), SEQ ID NO:15 (Ala5), SEQ ID NO:4 (Ala6), SEQ ID NO:5 (Ala7), SEQ ID NO:7 (Ala9), SEQ ID NO:8 (Ala13) and SEQ ID NO:10 (Leu)) are named.

Furthermore, 11 mutants comprising a mutation in the oligomerization domain, as recited in new claims 61, 66 and 74, are described on page 36, lines 8-18 (SEQ ID NO:2 (Ala1), SEQ ID NO:12 (Ala2), SEQ ID NO:13 (Ala3), SEQ ID NO:14 (Ala4), SEQ ID NO:15 (Ala5), SEQ ID NO:4 (Ala6), SEQ ID NO:5 (Ala7), SEQ ID NO:7 (Ala9) and SEQ ID NO:9 (Ala14)), and on page 14, line 5 (SEQ ID NO:3 (Ala4+5) and SEQ ID NO:10 (Leu)).

Additionally, the mutants listed in new claims 62, 68 and 72, which increase repression of transcription from the AL1 promoter, are described in Figure 3 (SEQ ID

In re: Hanley-Bowdoin et al.  
Attorney Docket No. 5051.458  
Application Serial No.: 09/289,346  
Filed: April 9, 1999

NO:15 (Ala5), SEQ ID NO:4 (Ala6), SEQ ID NO:5 (Ala7), SEQ ID NO:7 (Ala9), SEQ ID NO:12 (Ala2), SEQ ID NO:13 (Ala3), SEQ ID NO:14 (Ala4) and SEQ ID NO:6 (Ala8)), in Figure 6B (SEQ ID NO:8 (Ala13) and SEQ ID NO:9 (Ala14)) and on page 17, line 12 (SEQ ID NO:3 (Ala 4+5)).

New claims 60-77 as presented herein are believed to be free of the 35 U.S.C. § 112, first paragraph and second paragraph issues raised by the Examiner regarding previously pending claims 42-48 and 50-54 and are merely re-written versions of these claims which correctly recite the various mutants and identify each by a sequence identification number. It is believed that no new matter is presented with these new claims, nor are any new issues raised regarding the subject matter of the new claims as compared with the subject matter of the previously pending claims. Therefore, applicants respectfully request the entry of these new claims and their allowance to issue.

#### **VI. Rejoinder of new claims 78-86**

New claims 78-86 are added herein and support for the subject matter of these claims is found in the language of original claim 27 (now new claim 60, which depends from claim 42), original claim 28 (now new claim 61, which depends from claim 44), original claim 30 (now new claim 62, which depends from claim 46), original claim 37 (now new claim 63, which depends from claim 50), original claim 38 (now new claim 64, which depends from claim 52), original claim 39 (now new claim 65, which depends from claim 53), original claim 56 (now new claim 66, which depends from claim 42) and original claim 57 (now new claim 67, which depends from claim 50).

Applicants wish to remind the Examiner that, according to the rules of rejoinder as set forth in Section 821.04 of the MPEP, if allowable subject matter is found in the pending composition claims, then claims reciting methods directed to using the claimed compositions and having all of the limitations as set forth in the allowed claims are to be

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Application Serial No.: 09/289,346  
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rejoined and examined on the merits in the same application. Thus, applicants request the opportunity to introduce new claims 78-86 for examination in this application that are directed to methods of making a transgenic plant having increased resistance to geminivirus infection, comprising the use of the compositions of the pending claims.

For the foregoing reasons, applicants believe that all of the pending rejections have been adequately addressed and that the claims as presented herein are in condition for allowance. The Examiner is encouraged to contact the undersigned directly if such contact will expedite the examination and allowance of the pending claims.

A check in the amount of \$63.00 is enclosed for additional claim fees. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

Respectfully submitted,

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In re: Hanley-Bowdoin et al.  
Attorney Docket No. 5051.458  
Application Serial No.: 09/289,346  
Filed: April 9, 1999

## APPENDIX

### Marked-up version showing changes made

On page 23, please delete Table 3 and substitute therefor:

Name	Amino Acid substitution sites	SEQ. ID NO.
Alanine Substitutions		
Ala1	RS-R125	2
Ala2	QT130	<u>12</u>
Ala3	ND133	<u>13</u>
Ala4	E--N140	<u>14</u>
Ala4+5	E--N140 + KEE146	3
Ala5	KEE146	<u>15</u>
Ala6	REK154	4
Ala7	EKY159	5
Ala8	Q-HN165	6
Ala9	N-DR172	7
Ala10	K--E179	<u>16</u>
Ala13	FQ118	8
Ala14	D120	9
Leucine Substitutions		
Leu	AAA136	10

On page 39, lines 18-28, please delete the paragraph therein and substitute therefor:

--The ability of the mutants to repress AL1 promoter activity in vivo was studied. The AL1 promoter fused to the luciferase reporter gene (*lux*) was transfected into *N. benthamiana* protoplasts either alone or in the presence of plant expression cassettes for wild type and mutant AL1 proteins. In these experiments, wild type AL1 repressed transcription from the AL1 promoter approximately 20-fold. Repression mediated by mutant AL1 proteins [were] was standardized to the percent of wild type repression within each [experiments] experiment. All of the mutants that [were] reduced viral DNA



In re: Hanley-Bowdoin et al.  
Attorney Docket No. 5051.458  
Application Serial No.: 09/289,346  
Filed: April 9, 1999

replication (except for Ala1), also repressed promoter activity 2- to 4-fold higher than wild type AL1. DNA binding is required for repression and Ala1 is a DNA binding mutant. AL1 K—E179 (Ala10) supported normal replication levels and repressed the AL1 promoter similar to wild type AL1. Figure 6A (see lane 13) and Figure 6B.--